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Pediatric Medical Device Development Pathways

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Summary

- The Pediatric Medical Device Safety and Improvement Act (PMDSIA) was passed in 2007 to increase the number of pediatric devices approved by the Food and Drug Administration (FDA).
- PMDSIA also led to the introduction of the Pediatric Device Consortia grant program, which promotes institutions to pass new pediatric devices.
- In the past, people relied on nontraditional methods of gaining capital for medical device development.
- Since the act, pediatric devices have still lagged behind FDA-approved adult medical devices due to various clinical hurdles, including the small market size, which can result in a limited return on investment (ROI), a challenge for private investors.

Pediatric Medical Device Development Pathways

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Topic Relevance by Timeline

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Introduction

By definition, pediatric medical devices help to treat or diagnose conditions from birth to the age of 21. Medical device companies often steer away from products that are targeted toward pediatric populations—due to the small market size relative to adult populations—and from the unique needs of this patient group, which can result in additional costs and time for clinical trials. Thus there can be limited medical device treatment options for pediatric patients. To overcome these hurdles, several key initiatives have been launched to promote the development of pediatric medical devices. These programs, the unique pediatric regulatory considerations, and other

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opportunities/challenges will be discussed in this chapter. As with adult medical devices, applications for new pediatric devices must be reviewed by the FDA's Center for Devices and Radiological Health (CDRH), and pediatric medical devices are classified into three groups: class I, II, and III. (see the chapter on "FDA Device Regulation: 510(k), PMA").

FDA Initiatives

In 2009, the FDA began a grant program called the Pediatric Device Consortia (PDC) to promote the development, production, and distribution of pediatric medical devices by funding various nonprofits (Lai et al.). Since the launch of the program, different regional consortia have been funded: Atlanta, D.C., southern California, Philadelphia, Boston, and UCSF, amongst others.

Previously, in 2007, Congress had passed a bill called the Pediatric Medical Device Safety and Improvement Act (PMDSIA), which intended to increase the number of FDA approvals for pediatric devices (Jenkins et al.). The act had two parts: 1) to eliminate the profit restriction on devices under the Humanitarian Device Exemption (HDE) and 2) to provide grant money to nonprofit consortia to promote the development of pediatric devices. Before the act, companies could not profit from devices that were passed under HDE, i.e., high-risk devices that were approved due to the need for devices for rare diseases. By eliminating the profit restriction, companies had a new incentive to develop pediatric devices. As a result of the formation of the PDC, the consortia have led to the successful development of new pediatric devices.

The consortia bring together individuals, groups, or institutions that work jointly to develop new pediatric medical devices. The consortium grants are not awarded for specific devices. Rather, groups work together to address the clinical needs for developing pediatric medical devices, including the intellectual property (IP), business planning, regulatory advising, testing, and engineering involved (Lai et al.). The funding originates from the Office of Orphan Products Development, but the grant supports the development of all pediatric medical devices for both rare and common diseases. The FDA has awarded about $3.3 to $6 million each year to support the seven or eight consortia as shown in Table 1 (Office of the Commissioner).

Clinical Need and Hurdles

Before the act, there was little incentive for companies to develop new pediatric devices, due to the limited return on investment. According to the FDA, pediatric device development lags five to ten years behind adult device development. Oftentimes pediatric surgeons apply adult instruments to pediatric patients (Iqbal et al.). In some cases, these off-label uses of adult medical devices have led to adverse events (Hwang et al.). Additionally, when adult devices no longer maintain their profitability, the production is stopped even if they may have a beneficial pediatric use: for exam-

ple, the Linvatec arthroscopy knife was discontinued despite its potential use for pediatric populations (Iqbal et al.). Even if there is an individual clinician with a novel idea, there may be difficulty developing a product through the entire pediatric regulatory process. Developing a medical device includes building a prototype and manufacturing the device for clinical use, which may require outsourcing and can be costly (Iqbal et al.). The device must then be tested in vivo and in animal studies before the inventor or clinician can proceed to an investigational device exemption (IDE). Iqbal et al.'s 3MP IDE was 141 pages and took more than a decade to write. Thus, the medical device pathway is time-consuming and costly. The long regulatory pathway is specific to the U.S.; in comparison, the process of obtaining the Conformité Européenne (CE) mark requires simply that the investigator demonstrate that the device performs its stated function and is safe (Iqbal et al.). In Europe, investigators do not need to show randomized trial data, which is one of the regulatory hurdles in the U.S.

Table 1. PDC Funding from 2013 to 2017.

Year	PDC Grant Funding
2013	$3.6 million to support seven consortia
2014	$3.3 million to support eight consortia
2015	$3.55 million to eight consortia
2016	$4 million to seven consortia
2017	$6 million awarded to seven consortia

The main problem in the pediatric medical device industry is that there may not be enough support for inventors to see their product become approved and benefit society. The underlying issue with pediatric devices is that they serve a limited population, thus oftentimes many pediatric medical devices are categorized as orphan devices (Iqbal et al.). Companies may not want to treat diseases with low prevalence rates, due to the small return on investment and the negative press stemming from the price of treatment (Iqbal et al.). For example, Genzyme Corporation made a product to treat Gaucher's disease that cost $400,000 per patient annually. The patient size was 20,000 people in the U.S., which caused controversy for the company, as it was criticized for price gouging (Iqbal et al.).

In some cases, a company may choose to develop and produce a pediatric device out of altruism, and it may not bring a significant profit. For example, Covidien produced a uterine stapling device in 1984 to support the advent of open fetal surgery. Covidien still manufactures the product despite its limited profitability, in order to continue to support fetal surgeons (Iqbal et al.). Similarly, Karl-

Storz occasionally stops the manufacturing of its profitable adult line of surgical instruments in order to produce 3mm endoscopic instruments for pediatric surgeons (Iqbal et al.). Only 5%–6% of healthcare is actually spent on children, despite the fact that about 25% of the population are children, in large part due to the fact that most children are healthy. Thus, a specific device may only target a fraction of that 5%–6%, which makes pediatric devices potentially unprofitable (Barbella).

An illustrative example involves a businessman named Tim Moran, who took matters into his own hands when he faced difficulty finding support for medical devices for premature infants. Moran formed a nonprofit called PediaWorks Inc. at the Cleveland Clinic's business development center. He was personally motivated by his eldest child's premature birth and the lack of devices available for neonates. One vivid incident involved the distress his daughter experienced as the doctors strapped an extremely large airway mask to her head because it was the only one available. While Moran was experienced with the business side of his pediatric device company, no one was interested in investing, because, he was told, "it's not a market that we can justify to our shareholders" (Barbella). Moran was determined and ended up cold-calling a Japanese medical equipment firm, which ultimately invested $500,000 into his venture, and he was able to successfully develop pediatric catheters and sheaths. Moran's experience is a common one—companies or organizations interested in pediatric device development have had to rely on nontraditional financing based on "purpose rather than profit" (Barbella).

While the PDC has aimed to close the gap between clinical needs and the availability of pediatric devices, there remains considerable work to be accomplished. The PDC should continue to expand its consortia to other cities. One current limitation of the grant is that the institution must already have a well-established infrastructure for device development that includes clinical, scientific, and business arms (Iqbal et al.). However, there must also be greater capital investment beyond the PDC. That is, there needs to be a paradigm shift in the way the pediatric device world generates profit, and this would start with investors. Successful pediatric devices have often been funded by altruism or personal investment in a device. There needs to be more support for orphan devices that go beyond altruism and personal investment, although this would certainly be a long-term issue that requires time to resolve. Other solutions would be further government initiatives to promote industry involvement, in the form of grants or tax incentives (Iqbal et al.). Additionally, more programs can be created that focus on device innovation within medical and business schools, which may include training on IP and regulatory pathways (see the chapters "Intellectual Property: Ownership and Protection in a University Setting" and "Intellectual Property: Commercializing in a University Setting").

Another concern regarding the 2007 PMDSIA Act is that it has not led to as much innovation as expected for pediatric patients under the age of 18. In a 2014 study by Hwang et al., almost all the high-risk devices approved were indicated for pediatric patients above the age of 18. The devices were approved on the basis of a study with a small age range of patients (for 18- to 21-year-olds),

who are not normally considered pediatric (Hwang et al.). Thus the testing and approval of high-risk medical devices in pediatric populations under 18 is still uncommon, even after the passage of the 2007 act.

The Future of Medical Devices

While there are certainly regulatory hurdles that have set back medical device development, there is hope for a faster and more efficient regulatory process, which may ultimately lead to new pediatric devices. As recently as April 2018, FDA Commissioner Scott Gottlieb released a statement on the FDA's new efforts to modernize the medical device pathway (Gottlieb). Gottlieb announced the Medical Device Safety Action Plan, which outlined the FDA's efforts to update the regulatory process to help address unmet needs. One aspect of the action plan was the transition to a Total Product Life Cycle (TPLC) approach for product safety. TPLC is a database of pre- and post-market information, which the FDA will use to optimize decision-making (Gottlieb). The FDA also announced new programs and changes that include a revamped 510(k) pathway for efficient approval, as well as initiatives to address unmet medical needs (see the chapters "FDA Device Regulation: 510(k), PMA" and "Identifying Unmet Needs: Problems that Need Solutions"). While the recent announcement is hopeful, it will take time for the changes to be well studied and implemented.

Conclusion

Pediatric medical device development is challenging on several levels. Many previously approved pediatric devices have been developed through nontraditional methods of investment capital or because of individuals' and companies' altruism. The FDA has recently recognized this issue and has made progress toward modernizing the pediatric medical device pathway as well as continuing support for pediatric medical device development. This has created unique opportunities in terms of funding support and other modes of assistance that can allow for increased pediatric medical device development.

Resources

1. The list of different Pediatric Device Consortia are available on the FDA's website: https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/PediatricDeviceConsortiaGrantsProgram/.
2. An introduction into the PMDSIA and its impact are summarized here: http://pediatrics.aappublications.org/content/early/2016/12/22/peds.2016-3439.

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